

Normalization effect of preceding protein meals on "diabetic" oral glucose tolerance in Eskimos

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Summary: Routine testing of 76 clinically non-diabetic Eskimos showed marked impairment of oral glucose tolerance in 54% but normal intravenous glucose tolerance in most of these.

Total insulin output following the glucose drink was not found different in Eskimos with normal and abnormal glucose tolerance nor did lean meat meals given 60 minutes before the glucose significantly increase it.

Intolerance to oral glucose loads appeared significantly related to a delay of insulin release and both timing of insulin response and shape of blood glucose curve normalized in the meat-preceded tests.

Resumé: L'effet normalisateur d'un repas protidique préalable sur la tolérance "diabétique" à la glucose orale chez des Esquimaux

Au cours d'examens de contrôle courants chez 76 Esquimaux, non diabétiques sur le plan clinique, on a noté chez 54% des sujets une altération prononcée de la tolérance au glucose donné oralement, mais une tolérance normale chez la majorité des mêmes sujets par voie intraveineuse.

L'insulinémie globale après la boisson de glucose n'a pas été différente chez les Esquimaux dont la tolérance au glucose était anormale ou était normale, et le repas de viande maigre donné 60 minutes avant l'ingestion de glucose ne l'a pas augmentée sensiblement.

L'intolérance à la charge de glucose oral a paru nettement liée à un retard dans la libération d'insuline: le synchronisme à la réaction insulinaire et l'allure de la courbe glycémique se sont normalisés dans les épreuves comportant un repas protidique préalable.

In previous studies carried out in the Northwest Territories and at the Charles Camsell Hospital in Edmonton, Canadian Eskimos were shown to have an extremely low incidence of clinical diabetes mellitus despite the relatively frequent occurrence of intermittent glucosuria on a standard North American diet.^{1, 2} Random testing demonstrated that more than one half reacted abnormally to a standard oral glucose load while almost all showed normal tolerance to intravenous glucose administration.³ It was suggested that this marked and previously unreported discrepancy between oral and intravenous glucose tolerance might be explained by deficient release of an intestinal glucose-responsive insulinogenic hormone^{4, 5} in many Eskimos whose traditional diet was devoid of readily absorbable carbohydrates. In such individuals it was believed that aminogenic insulin release⁶ could be of greater physiological importance. Protein might stimulate sufficient insulin release to improve glucose tolerance in the meat-fed state, in contrast to the fasting state. The study presented here was designed to test this hypothesis and further assess "diabetes" in the Eskimo through the measurement of serum insulin values.

Materials and methods

Seventy-six ambulatory adult Eskimos (37 males, 39 females) were studied before their return North after hospitalization for various diagnostic and therapeutic reasons. Their mean age was 37.9 years and all age groups were well represented. None had any clinical stigmata of diabetes mellitus or other metabolic diseases. All had normal renal and hepatic function and their fasting blood glucose levels were less than 105 mg./100 ml. The degree of obesity was defined in each subject by adding skinfold thickness measurements from three sites (mid-triceps, subscapular and supra-iliac).

Following seven or more days on a diet containing at least 300 g. of carbohydrate and after an overnight fast, all subjects had a standard oral glucose tolerance test (OGTT), receiving 100 g. of glucose if their body weight was greater than 50 kg. and 75 g. if it was less than 50 kg.

Forty-one of the subjects were also tested in a meat-fed state (M+GTT). They were given 300 to 500 g. of lean

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hamburger 60 minutes before the glucose drink.⁷

Tests were performed at one-week intervals. Repeat OGTTs in 20 and an alternating sequence of OGTT and M+GTT in the first 26 subjects did not show any persistent trend attributable to test repetition. Thereafter we used OGTTs first in all subjects, selecting only those with abnormal results for M+GTTs.

Twenty-two subjects also had intravenous glucose tolerance tests (IVGTT), receiving 0.5 g./kg. glucose over two to four minutes.

Venous blood samples for serum immunoreactive insulin (IRI)⁸ and blood glucose determinations by Auto-Analyzer were collected before the glucose drink and every 15 minutes for 150 minutes thereafter during the OGTTs. During the M+GTT studies blood samples were collected in a similar manner, with additional samples before the meat meal and 45 and 60 minutes thereafter.

The total and post-glucose increments of area covered by the blood glucose and serum IRI curves were calculated by computer. Insulinogenic indices⁹ were determined according to the formula: increment of area covered by insulin curve (Δ IRI): increment of area covered by glucose curve (Δ Glucose). Glucose utilization constants (K_G) were derived from IVGTT values as described previously.³

Results

Forty-one of the 76 Eskimos (54%) showed definitely abnormal blood sugar curves when the standard OGTT was performed. This incidence is essentially the same as that reported by one of us in a larger series tested previously.

Details as to the degree of abnormality and sex distribution are set forth in Table I.

In the group with most markedly abnormal blood sugar

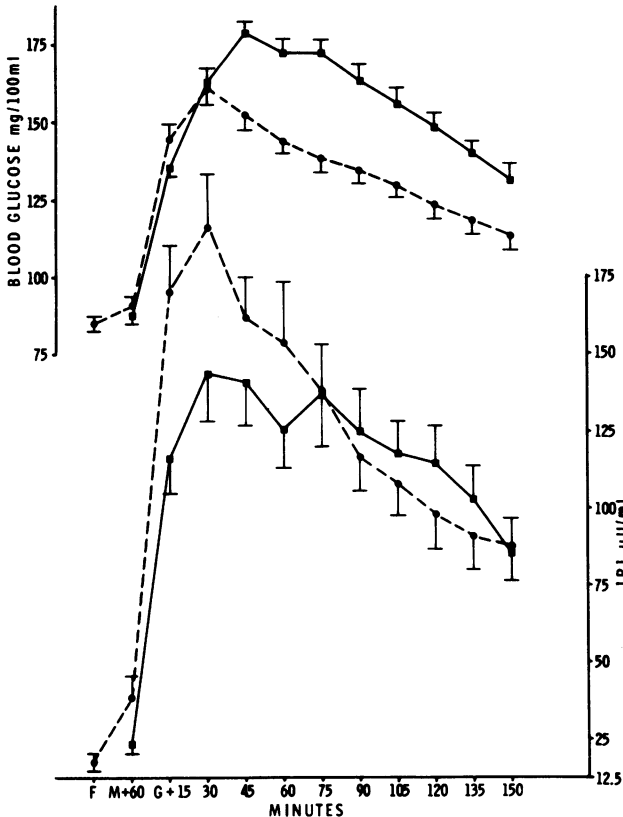


FIG. 1—Mean blood glucose and serum insulin levels in 41 Eskimos in fasting (●) and meat-fed (○) states.

curves females outnumbered males 14:5 while in the group with normal curves males exceeded females 10:6. This sex difference, which approached statistical significance ($0.1 > P > 0.05$), may be explained partly by the markedly greater obesity found in our female subjects and could not be attributed to minor differences in mean age. All 16 obese Eskimos (summed skinfold thickness exceeding 50 mm.) were females and the great majority of male Eskimos were quite lean (Table II). Although there appeared to be a relationship between degree of obesity and the degree of abnormality of OGTT it was not statistically significant ($P > 0.1$).

Multiparity was associated with a higher incidence of

Table I

Results of standard OGTT in 76 adult Eskimos

	Males		Females		Total	
	No.	Rate(%)	No.	Rate(%)	No.	Rate(%)
Grossly abnormal*	5	13.5	14	35.9	19	25.0
Moderately abnormal**12	32.4		10	25.6	22	28.9
Slightly abnormal***	10	27.0	9	23.1	19	25.0
Normal	10	27.0	6	15.4	16	21.1
Totals	37		39		76	

*Several values > 200 mg./100 ml. and/or

2-hr. value > 160 mg./100 ml.

**Several values > 175 mg./100 ml. and/or

2-hr. value > 140 mg./100 ml.

***Several values > 160 mg./100 ml. but none > 185 mg./100 ml. and/or 2-hr. value between 125 and 140 mg./100 ml.

Table II

Results of standard OGTT in relation to degree of obesity*

	> 50mm. 30 to 49mm. < 30mm.			Total
Grossly abnormal**	7 (all f)	3 (1m, 2f)	9 (4m, 5f)	19
Moderately abnormal**	3 (all f)	7 (3m, 4f)	12 (9m, 3f)	22
Slightly abnormal**	4 (all f)	7 (4m, 3f)	8 (6m, 2f)	19
Normal	2 (all f)	3 (0m, 3f)	11 (10m, 1f)	16
Totals	16 (all f)	20 (8m, 12f)	40 (29m, 11f)	76

*Expressed by sum of three skinfold measurements, over mid-triceps, below scapula and above crista iliaca.

**See definitions under Table I.

f-female, m-male.

Table III

Mean total blood glucose and insulin levels and insulinogenic indices during 150-minute test period following standard OGTT and timing of peak insulin response in 74 Eskimos

	No.	Total glucose area	Total insulin area	Insulinogenic index (Δ IRI) to glucose (Δ Gluc)	Time of peak insulin response to glucose drink in minutes
Grossly abnormal†	19	26,639 ± 653 ***	16,642 ± 2109 n.s.*	0.985 ± 0.118 **	87.6 ± 7.1 **
Moderately abnormal†	22	22,289 ± 205 ***	21,024 ± 2154 n.s.*	1.818 ± 0.185 n.s.*	46.4*** ± 4.8 n.s.
Normal and slightly abnormal†	33	18,953 ± 246	17,106 ± 1490	2.235 ± 0.201	40.9 ± 3.2

†See definitions under Table I

n.s.—not significant ($P > 0.2$)

n.s.*—not significant ($0.2 > P > 0.1$).

**—highly significant ($P < 0.001$).

***—extremely significant ($P < 0.001$)

abnormal OGTTs only when the number of pregnancies was nine or more.

Tables III and IV show the means for total blood glucose, IRI levels, insulinogenic indices and the timing of the maximal IRI values found during the OGTTs in 74 Eskimos grouped according to the degrees of glucose tolerance abnormality and obesity.

Subdividing each of the three obesity groups into those with "poor" (total glucose area >2300) and "fair" glucose tolerance (Table V), we see that only the grossly obese subjects with "poor" glucose tolerance have a diminished insulin output. Some of these people may be early diabetics. Borderline abnormal IVGTT results (K_G 0.8 to 1.0) in three of six from this group and progression to definite chemical diabetes in one of them 18 months later support this suggestion.

Analysis of IVGTTs, performed on a selected group of patients previously found to show varying degrees of

abnormality during the standard OGTTs, confirmed our findings in an earlier series.³ The mean K_G of the 22 IVGTTs was 1.45 ± 0.99 with only three in the borderline range of 0.80 to 0.99 and none in the range typical for diabetics (<0.80) despite the fact that results of OGTTs had been abnormal (14 grossly, six moderately, two slightly; mean total glucose area 24,909, none less than 21,500).

The limits of normal in oral and intravenous glucose tolerance test results have been determined mainly in Western Caucasian populations; employment of these standards for different races may be open to question. Despite the marked differences between IVGTT and OGTT results there is some consistency: subjects with lesser degrees of OGTT abnormalities had a mean K_G of 1.73 ± 0.11 while those with grossly abnormal OGTTs had a mean K_G of 1.29 ± 0.10 ($P < 0.01$). Insulinogenic indices in IVGTTs and OGTTs showed parallel trends (Table VI).

Of central interest to our investigation was the question of whether the abnormal glucose tolerance demonstrated in more than half of the Eskimos studied could be improved if the tests were preceded by a meat meal.

Fig. 1 and Table VII contrast the results of blood glucose and serum IRI measurements of OGTTs and M+GTTs in the 41 Eskimos who had both tests. Blood glucose levels did not change significantly one hour after protein ingestion while IRI levels increased to a barely significant degree ($P < 0.05$) from 18.2 ± 2.3 to 40.6 ± 6.7 μ U./ml. There were no significant differences in the blood glucose values until 45 minutes after glucose ingestion. At this time and for the duration of the test, glucose levels were significantly lower ($P < 0.001$) in the M+GTTs. In contrast serum IRI values were significantly higher during the M+GTTs at 15 and 30 minutes ($P < 0.01$ and $P < 0.05$ respectively) but not significantly different thereafter, tending to be higher in the M+GTTs up to 75 minutes and lower from then on.

Table VIII summarizes the Δ Glucose, Δ IRI and insulinogenic indices for the early (0 to 75 mins.) and late (75 to 150 mins.) phases of the tests. Preceding protein ingestion influenced Δ Glucose and Δ IRI to different degrees during early and late phases. Δ Glucose was more reduced in the late than in the early phase while Δ IRI was increased in the early and decreased in the late phase. For the entire 150 minutes there was a highly significant reduction of Δ Glucose while the total Δ IRI was almost

Table IV

Total blood glucose and insulin area, insulinogenic indices and timing of peak insulin response during standard OGTT in 74 Eskimos grouped according to degree of obesity

Degree of obesity	No.	Total glucose area	Total insulin area	Insulinogenic index	Time of peak insulin response in minutes
Grossly obese† (>50mm.)	16	23,038 ± 875 n.s.	17,731 ± 1933 n.s.	1.553 ± 0.210 *	64.7 ± 8.1
Mildly obese† (30-49mm.)	20	21,751 ± 959 n.s.	21,547 ± 2579 n.s.*	2.258 ± 0.253 *	57.0 ± 8.0 n.s.*
Lean† (<30mm.)	38	21,535 ± 600	16,543 ± 1338	1.643 ± 0.172	48.9 ± 4.2

†See footnote under Table II.

n.s.—not significant ($P > 0.1$).

n.s.*—not significant ($0.1 > P > 0.05$).

*—probably significant ($P < 0.05$).

Table V

Mean total blood glucose and serum IRI values and insulinogenic indices and times of maximal insulin response in OGTTs in 74 Eskimos grouped according to degree of obesity and degree of glucose intolerance

Degree of obesity†	Glucose tolerance‡	No.	Total glucose area	Total insulin area	Insulinogenic index	Time of maximal insulin response in minutes
Grossly Obese (> 50mm.)	Poor	8	25,878 ± 840	15,107 ± 2164	1.025 ± 0.184 **	82.5 ± 10.6 *
	Fair	8	20,198 ± 519	20,354 ± 3074	2.082 ± 0.276	46.9 ± 8.7
Mildly obese (30-49mm.)	Poor	4	28,244 ± 2730	29,879 ± 9143	1.879 ± 0.728	105.0 ± 18.4 **
	Fair	16	20,127 ± 454	19,463 ± 2215	2.353 ± 0.267	45.0 ± 6.0
Lean (< 30mm.)	Poor	15	24,835 ± 451	17,317 ± 2424	1.150 ± 0.182 **	65.0 ± 7.6 **
	Fair	23	19,382 ± 380	16,038 ± 1583	1.965 ± 0.238	38.5 ± 3.5

†See footnote Table II.

‡Poor—total glucose area > 23,000 during 150 minutes following glucose drink.

Fair—normal tolerance and lesser degrees of intolerance with total glucose area < 23,000.

* $P < 0.02$.

** $P < 0.01$.

Table VI

Results of OGTT in fasting and meat-fed state tests related to IVGTT

No.	IVGTT			OGTT		
	Level of K_G	Means ± s.e.m.	Insulinogenic index	Total glucose area	Insulinogenic index fasting test	Insulinogenic index meat-fed state test
6	< 1.20	0.962 ± 0.032	0.268 ± 0.056 n.s.	25,889 ± 1059 n.s.	0.990 ± 0.143 n.s.	2.105 ± 0.482 n.s.
7	1.20— 1.49	1.370 ± 0.033	0.329 ± 0.077 n.s.	25,309 ± 946 n.s.	1.223 ± 0.197 n.s.	1.961 ± 0.354 n.s.
9	> 1.50	1.837 ± 0.090	0.534 ± 0.089	23,945 ± 1522	1.882 ± 0.354	2.801 ± 0.498

*—Probably significant at $P < 0.05$.

n.s.—not significant ($P < 0.01$).

identical in OGTT and M+GTTs. The resultant insulinogenic indices were significantly increased in the M+GTTs during both phases but highest in the early phase.

Table IX presents data on changes in glucose increments, insulinogenic indices and times of maximal insulin response when M+GTTs are compared with OGTTs in 41 Eskimos grouped according to degree of obesity as well as degree of glucose intolerance in the OGTT.

The effect of preceding meat meals on glucose tolerance as measured by the glucose increment areas was very marked and of remarkably similar magnitude in all subjects with poorer degrees of performance in the OGTT. The effect was much smaller in those with better glucose tolerance. Obesity appeared to influence very little the effect of meat meals in this respect.

Insulinogenic indices in M+GTTs also increased more in those with "poor" glucose tolerance in the OGTTs.

Times of maximal IRI response following glucose drinks were quite similar in all subjects with fair OGTT results irrespective of skinfold thickness. IRI response was most markedly delayed in obese subjects with poor glucose tolerance in OGTTs; it advanced noticeably in all groups after M+GTTs, the maximal response occurring 20 to 30 minutes earlier.

Since the degree of changes effected by protein ingestion appeared strongly influenced by OGTT abnormality and very little by obesity, classification into three subgroups was made according to OGTT abnormality only (Table X). Thus it can be shown with more significant numbers that the corrective effect of protein ingestion on insulinogenic indices as well as on time of peak insulin response increases with degree of OGTT abnormality.

Discussion

An extremely low incidence of diabetes mellitus has been reported for the Eskimos of Canada,^{1, 2} Alaska^{10, 11} and Greenland,¹² in marked contrast to other Amerind races. Many North American Indian tribal groups have been shown to have very high rates of glucose intolerance.¹³⁻¹⁷ Somewhat lower rates have been found in Indians from the Eastern United States¹⁸ and Southern

Canada,¹⁹ but even these exceed age-adjusted rates of surrounding population communities. Alaskan Indians were reported to have rates almost as low as Alaskan Eskimos.²⁰

We have seen during the last few years a crop of new cases of diabetes in Indians and Eskimos living in the Mackenzie Delta where the change from native fare to imported food, with a marked increase in sugar consumption, preceded by almost 20 years similar developments in other parts of the Canadian Arctic. This must make one wonder when the entire population of Eskimos and Northern Indians will follow other Amerinds in their proneness to diabetes mellitus if subjected to modern man's fare. The findings of abnormal oral glucose tolerance in more than half of all adult Eskimos tested who were still by clinical criteria nondiabetic, and normalization or marked improvement of "diabetic"-appearing blood glucose curves when tests were conducted in the meat-fed instead of the fasting state, gain added relevance in view of the present consumption by younger Eskimos of large amounts of sucrose in food and drink taken

Table VIII
Increments of blood glucose and serum insulin and insulinogenic indices during early and late phases of OGTTs performed in 41 Eskimos in meat-fed and fasting state

	Time (minutes)	Fasting	Difference and significance of difference	Meat-fed
Blood glucose	0-75	5213 ± 258	-1239 P < 0.001	3974 ± 197
	75-150	4862 ± 361	-2208 P < < 0.001	2654 ± 232
	0-150	10075 ± 580	-3447 P < < 0.001	6628 ± 366
Serum insulin	0-75	7480 ± 677	+1627 P < 0.2	9107 ± 770
	75-150	6797 ± 734	-1557 P < 0.2	5240 ± 644
	0-150	14277 ± 1333	+70 P > 0.9	14347 ± 1283
Insulin index	0-75	1.572 ± 0.141	+0.974 P < 0.005	2.546 ± 0.260
	75-150	1.602 ± 0.176	+0.466 P < 0.05	2.068 ± 0.194
	0-150	1.574 ± 0.144	+0.769 P < 0.01	2.343 ± 0.209

Table VII
Effect of meat meal on glucose tolerance in 41 Eskimos tested in fasting and meat-fed state

Time (minutes)	Fasting	M + 60 FBS	15	30	45	60	75	90	105	120	135	150
Mean blood glucose												
OGTT		88.1	136.1	164.4	178.2	172.4	172.7	166.3	157.1	147.9	139.5	131.1
s.e.m.		1.154	2.372	3.433	5.025	5.595	5.383	5.573	4.868	4.787	4.375	4.537
M + GTT	86.5	92.1	144.5	161.6	153.4	144.5	139.2	135.5	129.4	122.9	118.7	114.3
s.e.m.	1.359	2.491	4.915	4.837	4.786	4.753	4.740	4.272	4.044	4.374	3.804	3.686
Significance of difference (P)												
		<0.2	<0.2	<0.7	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.01
Mean serum insulin												
OGTT		24.5	116.3	142.7	140.8	126.4	137.6	125.4	117.9	115.2	102.8	85.8
s.e.m.		4.091	11.794	14.395	13.443	12.882	16.843	14.173	10.768	12.309	10.411	9.031
M + GTT	18.2	40.6	170.8	192.5	162.2	155.1	139.2	117.4	107.7	97.6	92.0	86.9
s.e.m.	2.328	6.661	14.165	16.841	13.436	19.802	15.027	11.270	10.717	11.976	10.354	9.833
Significance of difference (P)												
		P≈0.05	<0.01	<0.05	<0.3	<0.3	>0.9	<0.7	≈0.5	≈0.3	0.5<P>0.4	>0.9

increasingly instead of or apart from meat meals.

We found that the most crucial factor in the degree and duration of hyperglycemia was the timing of the peak insulin response, while the total insulin output was not significantly different in Eskimos with normal and abnormal glucose tolerance.

In this regard Eskimos resemble Navajo Indians in whom Rimoin²¹ found insulin output to be in the same range as our values in Eskimos. He saw no difference between normal and mildly diabetic Indian subjects in contrast to the Pennsylvania Amish. It is noteworthy that the Navajos are relative newcomers to the Southwestern United States and were originally, with the other Athabaskan Indians, neighbours of the Eskimos.

Porte and Bagdade have suggested two pancreatic insulin pools: an acutely-releasable pool stimulated by the insulinogenic gut hormones and found defective in diabetics, and a chronic or delayed-response pool not affected by the gut hormones and usually unimpaired in maturity-onset diabetes.²²

Many Eskimos resemble mild diabetics in their delayed insulin response to orally administered glucose but they show in contrast to most diabetics a normal acute insulin release and normal glucose disappearance rate on intravenous testing. We therefore suggested previously that these Eskimos had a lower sensitivity of insulinogenic gut factors²³⁻²⁶ to glucose when given alone, and that this failure might be corrected with preceding meat meals.³

We found indeed "normalization" of glucose tolerance after protein ingestion as the consequence of earlier insulin release, possibly by "priming" the acutely-releasable insulin pool by amino acid-responsive insulinotropic enteric hormones such as pancreaticozym.

The gut mucosa may however not be the only site of regulatory weakness in those with abnormal OGTTs. Indeed some degree of parallelism of K-values in IVGTTs to OGTT results seen in a previous study³ and the present one, and a certain parallelism of insulinogenic indices in IVGTTs and OGTTs shown in Table VI suggest that the regulatory weakness of glucose metabolism in Eskimos and improvement with antecedent meat meals may involve factors not only at the gut mu-

cosa level but also in the pancreas and possibly elsewhere. Floyd *et al* demonstrated the direct action of infused amino acids on insulin release²⁷ and their synergistic action with glucose.²⁸

The traditional diet of Eskimos contained large amounts of proteins, lesser amounts of fat than generally assumed^{29, 30} and only small amounts of carbohydrate, mainly in higher complexed form as glycoproteins, and therefore not rapidly absorbable. Glucose and other rapidly absorbable mono- and disaccharides were for Eskimos less important factors than amino acids for the stimulation of insulin release. The failure to develop an elaborate regulatory mechanism to respond to sudden influx of glucose from the gut did not present a biological disadvantage to them until quite recently.

Acculturation has brought radical changes in nutritional habits to practically all Eskimos now, but the process started earlier and more gradually in Greenland, Alaska and more accessible western and southern regions of the Canadian Arctic. The way of living and diet were affected much later in the Canadian central and northern Arctic regions, but then more profoundly and at a more rapid pace. In one trading district, per capita sugar consumption quadrupled in eight years.

Regionally differing rates of growth-acceleration,³⁰ atherosclerotic diseases, diabetes mellitus and obesity

Table X
Influence of preceding meat meal on insulinogenic indices (Δ IRI/ Δ Gluc) and timing of insulin peak response of OGTTs in 41 Eskimos

Glucose curve results in fasting state	No.	Insulinogenic index		Time in minutes of peak insulin response	
		No. Fasting	Meat-fed	OGTT (fasting)	OGTT (meat-fed)
Grossly abnormal	16	1.10 ±0.21	* 2.02 ±0.34	85.3 +7.7	*** 46.9 ±7.1
Moderately abnormal	15	1.74 ±0.22	* 2.56 +0.34	48.0 +5.1	** 28.0 ±4.4
Normal or almost normal	10	2.09 ±0.32	2.49 ±0.46	48.0 ±8.3	28.5 +4.2
Total	41	1.57 ±0.14	** 2.34 ±0.21	62.6 ±4.9	*** 35.5 ±3.6

*P < 0.05 **P < 0.01 ***P < 0.001.

Table IX

Changes in glucose increments, insulinogenic indices and times of peak insulin response in MGTT and OGTT in 41 Eskimos grouped according to degree of obesity and degree of glucose intolerance in standard OGTT

Obesity	Glucose tolerance†	No.	Glucose increment area			Insulinogenic indices			Peak insulin response (minutes after glucose)		
			OGTT	M+GTT	% change	OGTT	M+GTT	% change	OGTT	M+GTT	% change
Grossly obese** (>50 mm.)	Poor (>23,000)	7	12,448 ± 949	7,381 ±1054	-41	0.890 ±0.144(*)	1.820 ±0.456	104.5	85.71 ±11.67	57.86 ±17.14	-32.5
	Fair (<23,000)	3	8037 ± 841	6900 ±911	-14	1.762 ±0.533	1.352† ±0.358	-23.3‡	35.00 ±13.23	25.00 ± 5.00	-28.6
Mildly obese** (30-49 mm.)	Poor (>23,000)	3	14,518 ±3338	8838 ±3240	-39	2.361 ±0.771	3.964 ±0.744	67.9	90.00* ±15.00	40.00 ±10.00	-55.6
	Fair (<23,000)	7	7278 ± 738	5514 ±340	-24	2.207 ±0.271	2.802 ±0.445	27.0	55.71* ± 9.66	30.00 ± 5.67	-46.1
Lean** (<30 mm.)	Poor (>23,000)	12	12,474 ± 630	6940 ± 588	-44	1.086 ±0.215(*)	1.736 ±0.259	59.9	68.75(*) ±8.35	45.00 ± 8.85	-34.5
	Fair (<23,000)	9	6513 ± 577	5669 ± 504	-13	1.938 ±0.349	2.997 ±0.542	54.6	43.33(*) ±7.26	23.33 ± 3.63	-46.2

(*) Not quite significant: 0.05 < P < 0.1

* Barely significant: P < 0.05

† As defined by total area covered by blood glucose curve in OGTTs during 150 minutes.

‡ Total insulin output (mean 19,758) was actually higher in the M+GTTs than OGTTs (mean 18,228). But a relatively higher elevation of baseline IRI values (up from 31 to 72 μ U/ml.) in these three subjects explains this paradox of total and increment-related IRI values in this small group.

** See footnote under Table II.

among Canadian Eskimo groups appear to parallel the history of nutritional change and in particular the history of sugar consumption.³¹ This may be related to excess stimulation of a number of hormones involved in the regulation of blood sugar levels, such as growth hormone, catecholamines, glucocorticoids and others besides insulin, caused by the wild blood sugar fluctuations to which Eskimos appear especially prone when consuming sugar loads.

These findings have immediate practical importance for preventive public health teaching and measures for Eskimos; but we suspect that the phenomenon of poor tolerance of oral loads of rapidly absorbable carbohydrates, improved by preceding protein meals, is not limited to Eskimos. The greater degree to which they demonstrate it probably reflects their former more exclusively carnivore diet. We found in a small number of Northern Bush Indians³² the same phenomenon, less consistently demonstrated. Comparative serial testing of intravenous and oral glucose tolerance in the fasting and meat-fed state of various populations with different racial and dietary backgrounds, including diabetic and non-diabetic persons, is necessary to substantiate the speculative views prompted by our findings in Eskimos or to put them into proper perspective.

It is of interest that D. Rabinowitz *et al* found in subjects tested in Baltimore, Maryland, that mixed protein-glucose loads elicited smaller fluctuations of blood glucose and growth hormone than either glucose or protein loads given alone.³³

The change from a carnivore to a mainly carbohydrate diet is a recent step in our evolutionary history. Some populations such as Eskimos are only now taking this step and metabolic-hormonal adaptations to this change may vary in different races. Refined sugar-products have been readily available for the last century; the shift from more complex and slowly absorbable carbohydrates to the simple and rapidly absorbable ones is now occurring fastest in such formerly carnivore populations as the Eskimos, who may be metabolically least well prepared for it.

For them and possibly many diabetics the sequence of events may start with a regulatory failure at the level of the gastrointestinal mucosa in the face of large loads of rapidly absorbable carbohydrate, for which dietary evolution has poorly prepared our organism. Undue stimulation of all or some of the endocrine organs involved in the regulation of blood sugar levels and eventual exhaustion — most notably of the insulin-producing organ — may be only secondary events.

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